Table 1. COMPARISON OF DISTANCES BETWEEN AMINO-ACID RESIDUES WHEN INSULIN AND GLUCAGON ARE ALIGNED AS IN FIG. 2, IN A FULLY EXTENDED CONFIGURATION

The distances are in angstroms and indicate the distances between α carbon atoms (refs. 3, 4)

Insulin (pig)		Glucagon	
Amino-acid	Distance (Å)	Amino-acid	Distance (Å)
His	0	His	0
Ser	3·6	Ser	3·6
Thr	23·2	Thr	21·7
Ser	26·9	Ser	25·3
Ser	37·7	Ser	36·2
Tyr	45·0	Tyr	43·5

confer slightly different activities cannot be determined with current methods. Biological assays indicate that insulin from different animals has about the same activity[6].

One possible test of the significance of the correlations pointed out here would be to assay the activity of glucagon after it has been cyclized to form a new peptide bond across the ends. Such a reaction should be possible with current synthetic methods. If the foregoing similarity between insulin and glucagon is significant with respect to their mode of action then it is expected that the cyclized form of glucagon would be biologically active.

This work was supported partly by a U.S. Public Health Service fellowship, *G.P.D.* 16,430, from the National Institutes of Health.

TODD M. SCHUSTER

Max-Planck-Institute for Physical Chemistry,
Göttingen, Germany.

[1] Sanger, F., Tuppy, E. O. P., and Kittai, R., *Biochem. J.*, **59**, 509 (1955).
[2] Bromer, W. W., Sinn, L. G., and Behrens, O. K., *J. Amer. Chem. Soc.*, **79**, 2807 (1957).
[3] Corey, R. B., and Pauling, L., *Proc. Roy. Soc.*, B, **141**, 10 (1953).
[4] Fieser, L. F., and Fieser, M., *Lehrbuch der organischen Chemie*, 1187 (tr. Hensel, H. R., Verlag Chemie, Weinheim, 1954).
[5] Harris, J. I., Sanger, F., and Naughton, M. A., *Arch. Biochem. Biophys.*, **65**, 427 (1956).
[6] Sanger, F., *Science*, **129**, 1340 (1959).

Effect of Age on Serum-bound Sialic Acid in Rats

CHANGES in the level of glycoproteins have been reported for a large number of conditions, primarily in man[1–6]. Since glycoproteins contain a number of sugar components for which quantitative methods are available, many of these methods have been used to estimate the serum- or plasma-bound carbohydrate. With the refinements of the thiobarbituric method[7] for a semi-specific assay of *N*-acetyl neuraminic acid, we have made use of this method to investigate the changes with age in the concentration of plasma-bound sialic acid in the rat in an initial effort to use experimental animals in the investigation of the physiological significance of glycoproteins.

Male Long–Evans Hooded Wistar rats were obtained from Simonsen Laboratories, Gilroy, California. After weaning, all animals were maintained on 'Purina' laboratory chow and water *ad libitum*. About 0·5–1 ml. of blood was obtained from the tail vein while the rats were under light ether anaesthesia. The blood was clotted and centrifuged and the serum was removed and stored at −40° C. Serum was diluted 1 : 50 and 1 : 30 in duplicates and hydrolysed in 0·05 N H_2SO_4 at 90° C for 30 min. *N*-acetyl neuraminic acid was determined by the Warren thiobarbituric method utilizing a known *N*-acetyl neuraminic acid preparation (an *N*-acetyl neuraminic acid of 95 per cent purity was obtained from Sigma Chemical Co., St. Louis, Missouri).

Data on the effect of age on serum-bound *N*-acetyl neuraminic acid are shown in Table 1. The results are

Table 1. EFFECT OF AGE ON THE LEVEL OF BOUND *N*-ACETYL NEURAMINIC ACID IN SERUM

Age	No. of animals	Percentage of the 6-month value
22 days	10	28·8 ± 7·60
31 days	10	33·5 ± 8·28
55 days	9	96·5 ± 18·57
6 months	8	100 ± 33·02
14 months	9	162·9 ± 28·70

expressed as the percentage of the 6-month value. The 6-month value was 125·1 ± 41·3 mg of *N*-acetyl neuraminic acid per 100 ml. of serum in reference to the commercial preparation. These data clearly demonstrate that there is an increase in the concentration of the acid-labile serum *N*-acetyl neuraminic acid with age. The function or physiological significance of this elevation in the level of serum sialic acid and the chemical identity of the augmenting fractions is now being investigated.

DAVID H. DAIL
JONAS E. RICHMOND

Department of Nutritional Sciences,
University of California,
Berkeley, California.

[1] Bettelheim-Javons, F. R., *Adv. Protein Chem.*, **13**, 36 (1958).
[2] Winzler, R. J., *Methods Biochem. Anal.*, **2**, 279 (1955).
[3] Goa, J., *Scand. J. Clin. Lab. Invest.*, **7**, Suppl. 22, 1 (1955).
[4] Biserte, G., *Bull. Soc. Chim. Biol.*, **39**, Suppl. III, 93 (1957).
[5] Schultze, H. E., *Scand. J. Clin. Lab. Invest.*, **10**, Suppl. 31, 135 (1957).
[6] Montreuil, J., *Bull. Soc. Chim. Biol.*, **39**, Suppl. III, 3 (1957).
[7] Warren, L., *J. Biol. Chem.*, **234**, 1971 (1959).

Role of Lysosomes in Adrenal Necrosis caused by Dimethylbenzanthracene

IT has long been recognized that carcinogenic chemicals, including polybenzenoid hydrocarbons, have injurious effects on cells[1,2]. Evidence has been presented that polybenzenoid hydrocarbons are concentrated in the lysosomes of living cells and the suggestion was made that release of lysosomal enzymes may play an important part in their cytotoxic action[3]. The necrosis of rat adrenal cortical cells produced by 7,12-dimethylbenz(*a*)anthracene (DMBA)[4] provided an opportunity to test this hypothesis in more detail, because it is specific in two ways. First, the degeneration is organ specific, adrenal cortical cells of the rat being much more sensitive than the cells of other organs. Secondly, it appears to be specifically produced by one compound, 7-hydroxymethyl-12-methylbenz(*a*)-anthracene (7-OHM-12-MBA), which is a metabolite of DMBA: an isomeric metabolite, 12-hydroxymethyl-7-methylbenz(*a*)anthracene (12-OHM-7-MBA), does not produce adrenal damage[5]. Rats can be protected against adrenal damage after administration of DMBA by previous treatment with a number of aromatic hydrocarbons and amines, which diminish the formation of 7-OHM-12-MBA from DMBA[5]. Hence it seems that the metabolite is more active than the parent compound in producing adrenal necrosis.

In order to ascertain whether there is any relationship between *in vivo* damage and release of lysosomal enzymes, particulate fractions of organelles from rat adrenals, kidneys and livers were prepared. In the case of the adrenal and kidney, the whole mitochondrial fraction, prepared by centrifugation of homogenates at 10,000*g* for 15 min, was used. The *F*3 fraction, a partially purified lysosomal preparation from rat liver, was used for comparison. This preparation, which was obtained by a sucrose layering technique, showed a twelve-fold increase in specific acid phosphatase activity as compared with the whole mitochondria preparation. The suspensions, adjusted by a standard turbidity (E_0 (500 mμ), 2·0) were incubated in 0·25 M sucrose buffered with 0·02 M *tris* *p*H 7·4. The carcinogen was dissolved in dimethyl sulphoxide (DMS) and added at the beginning of incubation. The